## Remarks

Claim 93 is amended, and claims 77 and 90 are canceled. Claims 65, 69, 73, 80, 83-89, 91, and 93 are now pending in this application.

The cancellation of claims 77 and 90 obviates the objection to those claims under 37 C.F.R. § 1.75.

The Examiner rejected claim 93 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner asserts that the phrase "at risk of" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. The Examiner also rejected claim 93 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (a "new matter" rejection). In particular, the Examiner asserts that the specification does not provide support for inhibiting leukocyte recruitment or migration in a mammal at risk of leukocyte recruitment or migration. These rejections are respectfully traversed.

With regard to the metes and bounds of the phrase "at risk of," it is Applicant's position that that the phrase is conventional and understood by the art. Evidence that "at risk" is a phrase understood by the art is provided in the definition of "risk factor" in Churchill's Medical Dictionary (Churchill Livingstone Inc., 1989, pages 675-678 are included herewith): "[i]n epidemiology, an attribute or circumstance associated with an enhanced risk of developing or of dying from a specific disease" (emphasis added). Moreover, documents provided to the Examiner with the Amendment filed on September 25, 2003 clearly evidence that risk factors for many indications including those associated with leukocyte migration and recruitment are known, i.e., one of ordinary skill in the art would understand whether a mammal was at risk of leukocyte recruitment or migration. For instance, individuals exposed to and having an aberrant sensitivity to house dust mites or pollen are at risk of acute dermal hypersensitivity, as mentioned in the Amendment filed on August 2, 2004.

Accordingly, the metes and bounds of the phrase "at risk of" in the context of the claims are definite.

With regard to support for inhibiting leukocyte migration or recruitment in a mammal at risk of leukocyte migration or recruitment, the Examiner is requested to consider page 18, lines 9-16 and page 98, lines 6-9 of Applicant's specification, where it is disclosed that the invention provides a method of preventing or inhibiting an indication associated with chemokine-induced activity in which an agent of the invention, e.g., a chemokine peptide, is administered to a mammal afflicted with or at risk of the indication. Page 30, lines 26-29 discloses that chemokines act on cells including macrophage, B cells, T cells, neutrophils and eosinophils, by affecting their migration. At page 22, lines 3-11, it is disclosed that the invention includes a method of preventing or inhibiting an indication associated with monocyte, macrophage, neutrophil, B cell, T cell or eosinophil recruitment.

In addition, Example 9 in the specification describes an animal model for dermal inflammation. As noted above, there are individuals known to be at risk of acute dermal hypersensitivity, e.g., due to prior exposure and acute reaction to an antigen. Example 9 discloses that administration of an agent of the invention prior to an event that causes dermal inflammation, e.g., MCP-1 or LPS administration, resulted in the absence (for MCP-1 induced inflammation) or reduced (for LPS induced inflammation) monocyte/macrophage recruitment. Further, Example 11 discloses an animal model for asthma. Mice were sensitized to an antigen (ovalbumin), i.e., the mice are at risk of an aberrant sensitivity to a particular antigen. Prior to challenge, an agent of the invention was administered to those mice. It is disclosed that reduced leukocyte recruitment was observed in treated animals.

Thus, the inhibition of leukocyte recruitment or migration in a mammal at risk of leukocyte migration or recruitment is described in the specification.

Accordingly, withdrawal of the § 112 rejections is respectfully requested.

*Conclusion*

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (612) 373-6959 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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Date February 15, 2005 By

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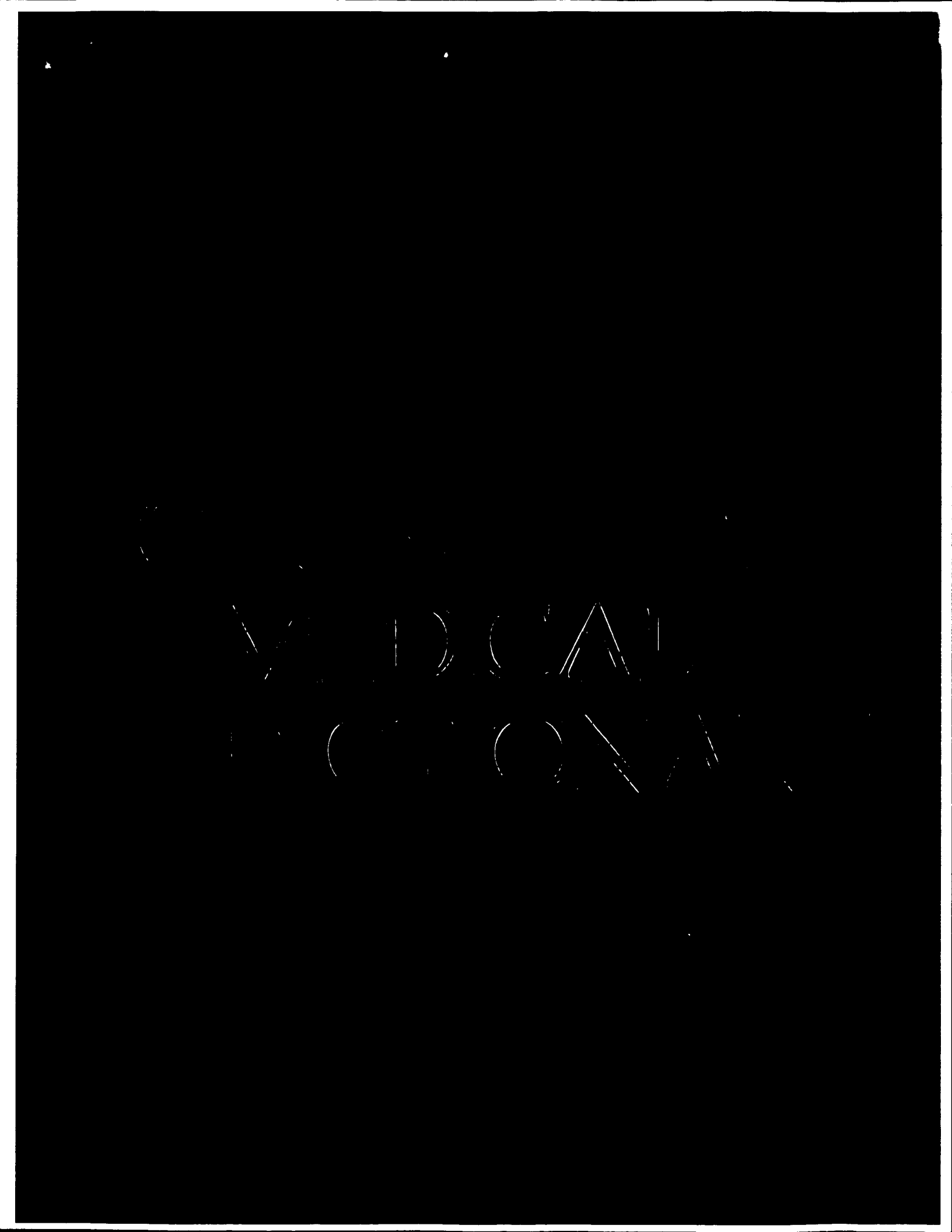

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and the pelvic surface, lying between the inferior margin of the auricular surface and the superior margin of the greater sciatic notch and forming part of the wall of pelvis minor. Also *sacropelvic surface of ilium.* **f. scaphoidea** A face that appears concave in profile, due to a protruding forehead, depressed nose and upper jaw, and a prominent chin. Also *dishface deformity.* **f. sternocostalis cordis** [NA] The anterior surface of the heart, facing anterosuperiorly and to the left and formed partly by the right atrium above and to the right and mainly by the ventricles, two-thirds by the right and one-third by the left. Also *sternocostal surface of heart.* **f. superior hemispherii cerebelli** The rostral, superior face of the cerebellum, consisting essentially of those portions rostral to the horizontal cerebellar fissure. **f. superior trochleae tali** [NA] The broad upper surface of the talus, widest anteriorly, convex anteroposteriorly, and concave from side to side, that articulates with the inferior articular surface of the tibia in the ankle joint. Also *superior surface of talus.* **f. superolateralis cerebri** [NA] The outer convex surface of the cerebral hemispheres underlying the calvaria. Also *facies convexa cerebri.* **f. symphysialis** [NA] The elongated, oval medial surface of the body of the pubis that articulates with the opposite pubis in the symphysis pubis. Also *symphysial surface of pubis.* **tabetic f.** Bilateral ptosis with compensatory wrinkling of the forehead seen in some cases of advanced tabes dorsalis. **f. temporalis alae magnae** FACIES TEMPORALIS ALAE MAJORIS. **f. temporalis alae majoris** [NA] The convex outer, or lateral, surface of the greater wing of the sphenoid bone, divided by the horizontal infratemporal crest into a large upper part, a portion of the temporal fossa, and a small lower part, a portion of the wall of the infratemporal fossa. • Some textbooks refer to the upper part as the temporal surface, and to the lower part as the infratemporal surface of the greater wing of sphenoid bone. **f. temporalis ossis frontalis** [NA] A small concave area posterior to the temporal line on the lateral aspect of the frontal bone that helps to form the wall of the temporal fossa. Also *temporal surface of frontal bone.* **f. temporalis ossis zygomatici** [NA] A small concave area facing posteromedially on the zygomatic bone, the posterior part of which extends upwards on the frontal process to form the anterior boundary of the temporal fossa. A backward extension on the medial part of the temporal process helps to form the lateral wall of the infratemporal fossa. The surface has a foramen for the zygomaticotemporal nerve. **f. temporalis partis squamosae** [NA] The large, convex anterior portion of the outer surface of the squamous part of the temporal bone that participates in the posterior part of the wall of the temporal fossa. **typhoid f.** The facial appearance characteristic of typhoid fever, marked by moderate flushing, lustrous and sunken eyes, a vacant, apathetic expression, and ashen color. Also *facies typhosa.* **f. urethralis penis** [NA] The inferior surface of the penis, in apposition with the scrotum and opposite to the dorsal aspect of the penis. **f. vesicalis uteri** [NA] The normally flattened anterior surface of the body of the uterus, in apposition with the urinary bladder from which it is separated by the vesicouterine excavation, or peritoneal pouch. **f. visceralis hepatis** [NA] The surface of the liver that faces inferiorly and posteriorly and is covered by peritoneum, except over the fossa for the gallbladder, at the porta hepatis, and in the fissure for ligamentum teres. It is divided into the right, left, and quadrate lobes, which are closely related to adjacent abdominal organs, such as the right kidney, stomach, transverse colon, gallbladder, and duodenum. Also *visceral surface of liver, inferior surface of liver.* **f. visceralis splenis** [NA] The medial surface of the spleen. It faces the abdominal organs and is divided into facies colica, facies gastrica, and facies renalis, which are related to the left colic flexure, the stomach, and the left kidney, respectively. The hilum of the spleen is situated on the gastric surface. Also *visceral surface of spleen.*

**facilitation** \fəsil′itā′shən\ [*facilit(y)* + -ATION] The neural process of enhancing or promoting synaptic events or reflex actions whereby the sum of separate inputs is additive. **associative f.** That process by which one association, already established, makes it easier to form another association to one of its elements. Thus, having already established an association between moon and June, an association between moon and spoon (or June and spoon) would be facilitated. **proprioceptive neuromuscular f.** The use of proprioceptive stimuli and reflex patterns to enhance contraction or relaxation of muscles. **f. of reflexes** REINFORCEMENT OF REFLEXES. **Wedensky's f.** The additive effect of an appropriately timed sequence of electric shocks, resulting in greater amplitude of muscle contraction than with a single shock of the same strength.

**facilitatory** \fəsil′ətətôr′ē\ Producing or promoting facilitation.

**facility** \fəsil′itē\ [L *facilitas* (from *facilis* easy to do, easy, from *facere* to make, do + *-itas* -ITY) readiness, easiness] A physical plant, along with its equipment and supplies, in which services are provided. **extended care f.** An inpatient health care facility providing skilled nursing and related services for long-term stays not appropriate to community hospitals. **intermediate care f.** A health care facility that provides inpatient care that is less complex or sophisticated than that of a general or community hospital or a skilled nursing facility but which is required by patients needing long-term institutionalization because of their mental or physical condition. **skilled nursing f.** An inpatient health care facility which provides care for patients that do not require the services of a community hospital but do require nursing care due to injury, disability, or mental health problems.

**facing** The visible tooth-colored part of a combined metal/nonmetal crown or unit of a prosthesis.

**facio-** \fā′shē·ō-\ [L *facies* face] A combining form denoting the face.

**facioplegia** \fā′shē·ōplē′jə\ FACIAL PARALYSIS.

**factitious** \faktish′əs\ Not occurring naturally; artificial or contrived.

# factor

**factor** [L (from *fact(us)*, past part. of *facere* to make, do + *-or* -OR), a maker, doer] 1 Any agent or element which helps to produce a result, as in an enzyme reaction, blood coagulation, or hormonal change. 2 A determinant of a mendelian character; a gene. An outmoded usage. **f. I** FIBRINOGEN. • The I in this term represents the roman numeral for 1, not the letter I. **f. II** PROTHROMBIN. **f. III** *Rare* THROMBOPLASTIN. **f. IV** The calcium present in plasma. *Seldom used.* **f. V** The coagulation factor that, when activated, is the cofactor of factor Xa in the formation of prothrombinase. Also *labile factor* (obs.), *proaccelerin, accelerator globulin, cofactor V, accelerator factor.* **f. VI** The original designation for activated factor V (accelerin). This term is no longer applied to any coagulation fac-

tor. **f. VII** A plasma coagulation factor intermediate in the clotting cascade. It dominates the "extrinsic" coagulation pathway. Also *stable factor, proconvertin, serum prothrombin conversion accelerator* (outmoded), *kappa factor, cothromboplastin.* **f. VIII** A plasma coagulation factor whose inherited deficiency is responsible for classic hemophilia (lack of factor VIII: C) or von Willebrand's disease (lack of factor VIII R: Ag). It is deficient in acute disseminated intravascular coagulation. Also *antihemophilic factor, antihemophilic factor A, hemophilic factor A, platelet cofactor I, thromboplastic plasma component, antihemophilic globulin* (original term). **f. VIII:c** The coagulant moiety of the factor VIII complex, having a molecular weight of about 250 000. This is primarily deficient in classic hemophilia. **f. VIII:CAg** The plasma protein that normally has factor VIII:C coagulant activity. Patients with or without hemophilia who develop anti-factor VIII antibodies do so against factor VIII:CAg. **f. VIIIR:Ag** The noncoagulatnt portion of factor VIIIR:Ag, which is necessary for platelets to adhere to damaged endothelium. This accounts for the long bleeding time in patients with von Willebrand's disease, who have a deficiency of this factor. This factor must also be present in adequate amounts in order for the antibiotic ristocetin to clump platelets. Also *Willebrand factor, transhemophilin, ristocetin cofactor, ristocetin factor, factor VIII T.* **f. VIII T** FACTOR VIIIR:AG. **f. IX** A plasma coagulation factor that may be deficient on an inherited basis (hemophilia B), or an acquired basis (vitamin K deficiency). Also *plasma thromboplastin component, Christmas factor, platelet cofactor II, autoprothrombin II, antihemophilic factor B, hemophilic factor B.* **f. X** A vitamin K-dependent plasma coagulation factor. When activated (factor Xa) it combines with activated factor V (factor Va) plus calcium and phospholipid to form the prothrombinase complex. Also *Stuart factor, Prower factor, Stuart-Prower factor, autoprothrombin I.* **f. XI** A plasma coagulation factor that forms the bridge between the activation factors, such as factor XII, and the hemophilic factors, factors IX and VIII. Deficiency of factor XI causes a bleeding tendency. Also *plasma thromboplastin antecedent, antihemophilic factor C, hemophilic factor C.* **f. XII** One of the activation factors initiating the intrinsic coagulation pathway. There is no bleeding diathesis when this factor is deficient. Also *Hageman factor, glass factor.* **f. XIII** An enzyme of blood plasma that cross-links strands of fibrin monomers, thus creating a mesh of polymerized fibrin and stabilizing the blood clot. Also *fibrin stabilizing factor, fibrinase, fibrinoligase, Laki-Lorand factor.* **accelerator f.** FACTOR V. **activated clotting f.'s** Products with clotting activity generated from the inactive plasma clotting proteins during the coagulation process. The inactive proteins have been assigned Roman numerals, and the active products have an *a* appended. Thus proaccelerin is factor V and accelerin is factor Va. **activation f.** Any of three plasma coagulation factors that, when activated, initiate the intrinsic clotting cascade. They are factor XII, prekallikrein (Fletcher factor), and high-molecular weight kininogen (Fitzgerald factor). Bleeding does not result from deficiencies of these factors. Also *contact activation factor.* **amplification f.** The ratio of output voltage to input voltage in the operation of an electronic or other amplifier, or one of its components. In a pulse amplifier this factor is equal to the voltage at the peak of an output pulse divided by that at the peak of the corresponding input pulse. **animal protein f.** VITAMIN $B_{12}$. **antiacrodynia f.** VITAMIN $B_6$. **antialopecia f.** INOSITOL. **antianemia f.** VITAMIN $B_{12}$. **antiberiberi f.** THIAMIN. **anti-black-tongue f.** NIACIN. **anticanities f.** PANTOTHENIC ACID. **antidermatitis f. of chicks** PANTOTHENIC ACID. **antidermatitis f. of rats** VITAMIN $B_6$. **anti-egg-white f.** BIOTIN. **antihemophilic f.** FACTOR VIII. **antihemophilic f. A** FACTOR VIII. **antihemophilic f. B** FACTOR IX. **antihemophilic f. C** FACTOR XI. **antihemorrhagic f.** VITAMIN K. **antineuritic f.** THIAMIN. **antipellagra f.** NIACIN. **antirachitic f.** VITAMIN D. **antiscorbutic f.** VITAMIN C. **antisterility f.** VITAMIN E. **antixerophthalmia f.** VITAMIN A. **atrial natriuretic f.** A heart atrial extract which produces marked natriuresis and diuresis when injected into rats. A synthetic form has been produced. **f. B** The component of the alternative complement pathway that is the homolog of C2 in the classical pathway. It is the zymogen of a complex serine protease. Factor B complexes with C3b in the presence of magnesium ions and is then cleaved by factor D to give rise to two products, Ba and C3b,Bb, the latter being the C3-converting enzyme of the alternative complement pathway. **backscatter f.** The ratio of the exposure or of the absorbed dose at a point on the surface of a patient or phantom to the exposure or absorbed dose due to primary photons only. **Bittner milk f.** MOUSE MAMMARY TUMOR VIRUS. **buildup f.** In a beam of high energy x rays or gamma rays the ratio of the peak absorbed dose to the surface absorbed dose. **calibration f.** A multiplier applied to the numerical reading of an instrument to convert a quantity with one physical dimension to a more informative one, for example counts per second to millicuries of radioactivity. **CAMP f.** A product of group B streptococci, seen when streptococci are grown on a blood agar plate near a hemolytic strain of *Staphylococcus aureus.* The factor enlarges the zone of $\beta$-hemolysis that surrounds the streaked colonies of *S. aureus.* **Castle's f.** INTRINSIC FACTOR. **chick antipellagra f.** PANTOTHENIC ACID. **chick growth f.** STREPTOGENIN. **chick growth f. S** STREPTOGENIN. **Christmas f.** FACTOR IX. **clearing f.** LIPOPROTEIN LIPASE. **clumping f.** Surface-bound coagulase of *Staphylococcus aureus,* which causes clumping in plasma by reaction with fibrinogen. **C3 nephritic f.** An autoantibody present in the plasma of some patients with membranoproliferative glomerulonephritis who have low plasma complement activity. The autoantibody has specificity for the C3b,Bb complex of the alternative pathway of complement activation, and it stabilizes the system for enzymatic cleavage of C3 to C3a and C3b. **coagulation f.'s** Any of the plasma proteins in the coagulation cascade plus calcium and thromboplastin. **conglutinogen-activating f.** FACTOR I. **contact activation f.** ACTIVATION FACTOR. **cord f.** 6,6'-Dimycolyl trehalose, a component of the cell envelope of *Mycobacterium tuberculosis* that promotes virulence and serpentine growth. **coupling f.'s** Substances which allow, or restore, mitochondrial oxidation to bring about phosphorylation so that adenosine triphosphate can again be produced, especially in mitochondria in which these processes have been uncoupled. **cow manure f.** VITAMIN $B_{12}$. **f. D** A serine protease of molecular weight 25 000 daltons which occurs in fully active form in plasma and is an essential component of the alternative pathway of complement activation. It cleaves Fb when this protein is bound to C3b. **decapacitation f.** A factor that prevents capacitation of spermatozoa, such that the ability of spermatozoa to fertilize an ovum is impaired. **decay accelerating f.** An erythrocyte membrane protein which functions as a control protein of the complement system. It accelerates the decomposition of C4b,2b, the C3-converting enzyme of the classical

pathway, into its components. Decay accelerating factor is absent on the abnormal erythrocytes of patients with paroxysmal nocturnal hemoglobinuria. **depolarization f.** The process of decreasing the membrane potential of a cell by any course in which the absolute potential value becomes less negative. **Duran-Reynals f.** **duty f.** Pulse duration multiplied by pulse repetition frequency. For example, in ultrasonography the pulse duration of 1 μs and a pulse repetition frequency of 2000 pulses/s yields a low duty factor of 0.002. **elongation f.** One of several cytoplasmic proteins that function cyclically during each addition of an amino acid in polypeptide chain elongation. In bacteria EFTu complexes with aminoacyl-tRNA and GTP to form a ternary complex that binds to the ribosome in the recognition step. EFTu-GDP is released and then interacts with EFTs, which leads to replacement of the GDP by GTP. EFG, complexed with GTP, participates in the translocation step in chain elongation, and it is released after hydrolysis of the GTP. In eukaryotic systems similar factors are called EF-1 and EF-2. **eluate f.** VITAMIN $B_6$. **eosinophil chemotactic f.** A lymphokine that, when activated by immune complexes, attracts blood eosinophils to sites of inflammation. **epidermal growth f.** A protein substance, extracted from submaxillary glands of male mice, which when administered to immature mice induces more rapid eyelid opening, eruption of teeth, and growth of epidermal structures. Larger doses may inhibit these processes. **essential food f.'s** Substances that are required by the body to sustain life but which cannot be synthesized by the body and so must be supplied exogenously by the diet. Such substances include linoleic acid, the vitamins and minerals, and the essential amino acids, specifically tryptophan, phenylalanine, lysine, threonine, valine, methionine, leucine, and isoleucine. Histidine is an essential amino acid during childhood. **extrinsic f.** VITAMIN $B_{12}$. **F f.** A particular plasmid that codes efficiently for transfer of itself, and also of the bacterial chromosome, by conjugation. This plasmid is the one with which bacterial conjugation was discovered in *Escherichia coli*. It is unusually efficient because it lacks a gene, present in most conjugative plasmids, that represses the transfer operon. Also *F plasmid, F agent, fertility factor.* **fertility f.** 1 F FACTOR. 2 Any conjugative plasmid. **fibrin stabilizing f.** FACTOR XIII. **filtrate f.** PANTOTHENIC ACID. **Fletcher f.** The original term for PREKALLIKREIN. • *Fletcher* was the name of the family in which an inherited deficiency of this factor was discovered. **F-prime f.** An F factor that has incorporated specific host genes and thus mediates their high-frequency transfer by conjugation. **Fy f.** The gene responsible for expressing the red cell phenotype Fy(a-b-) which is commonly found in blacks and rarely in whites. The Fy factor is so named because it is part of the Duffy blood group. **G f.** G FACTOR OF SPEARMAN. **general f.** G FACTOR OF SPEARMAN. **glass f.** FACTOR XII. **growth f.** 1 Any factor essential to skeletal or somatic growth, such as vitamin D, minerals, or the growth hormone. 2 A substance that is required for or that enhances growth of a particular microbe. Most growth factors are nutrients utilized by the cell, but some, as albumin or starch, are protective, acting by binding toxic compounds, especially soap, in the medium. **growth hormone inhibitory f.** SOMATOSTATIN. **G f. of Spearman** A unitary factor said to underlie performance scores earned on virtually all tests of mental ability and to contribute to and be responsible for the tendency for all cognitive measures to be positively related. Individuals are held to possess this general factor of mental ability in varying amounts, and it is to this ability to reason, to perceive relationships, and to educe correlates from them that reference is made when speaking of the individual's intelligence. Also *G component, general ability, general factor, G factor.* **f. H** 1 BIOTIN. 2 One of the control proteins of the complement system. Factor H binds to C3b and allows its cleavage by factor I. **Hageman f.** FACTOR XII. **hemophilic f. A** FACTOR VIII. **hemophilic f. B** FACTOR IX. **hemophilic f. C** FACTOR XI. **H f. of Lewis** The substances liberated into the skin after rubbing with a blunt instrument as part of the triple response of Lewis. It was presumed by Lewis, probably correctly, to be histamine with or without other pharmacologically active substances. **human f. IX complex** A fraction prepared from the supernatant plasma after precipitating human antihemophilic globulin. It is a concentrated mixture of coagulation factors II, VII, IX, and X, and it is used to treat bleeding episodes in patients with hemophilia B. **f. I** One of the control proteins of the complement system. It is a serine protease occurring in fully active form in plasma which cleaves C3b to iC3b. This reaction is of central importance in the control of the alternative complement pathway. Factor I will also cleave iC3b to C3c and C3dg; and C4b to C4c and C4d. All factor I cleavage requires the substrate to be bound to a substrate modifying protein. Also *C3b inactivator, conglutinogen-activating factor.* • The *I* in this term represents the letter I, not the roman numeral. **IgG rheumatoid f.** Immunoglobulin G with antibody activity against the Fc portion of a normal immunoglobulin G molecule. **IgM rheumatoid f.** The classic rheumatoid factor, consisting of an immunoglobulin M molecule with antibody activity directed against the Fc portion of a normal immunoglobulin G molecule. **initiation f.** One of several protein factors that participate in the initiation step in protein synthesis and then are released from the ribosome as it moves on into chain elongation. Bacteria have three initiation factors (IF-1, IF-2, IF-3). Eukaryotic cells have a larger number. **insulin-antagonizing f.** Any nonhormonal insulin antagonist, such as a fatty acid. **intermediate lobe inhibiting f.** MELANOCYTE STIMULATING HORMONE INHIBITORY HORMONE. **intrinsic f.** A glycoprotein of molecular weight in the order of 50 000 which is produced by normal gastric parietal cells. It dimerizes when it combines with vitamin $B_{12}$ to give a complex consisting of two molecules of intrinsic factor and two molecules of vitamin $B_{12}$. In this form $B_{12}$ is permitted to enter ileal mucosal cells. Deficiency of intrinsic factor impairs the absorption of $B_{12}$. This is common in old people. Also *Castle's factor.* **kappa f.** 1 A large, complex particle composed of DNA, RNA, and protein, occurring in the cytoplasm of certain strains of paramecia. Strains having kappa particles produce toxic materials which kill sensitive strains of paramecia. 2 FACTOR VII. **labile f.** *Obs.* FACTOR V. **lactogenic f.** *Outmoded* PROLACTIN. **Laki-Lorand f.** FACTOR XIII. **LE f.** ANTINUCLEAR ANTIBODY. **LE cell f.** ANTINUCLEAR ANTIBODY. **letdown f.** *Outmoded* PROLACTIN. **lethal f.** LETHAL ALLELE. **leukocyte migration inhibition f.** A lymphokine that inhibits migration of polymorphonuclear leukocytes. **leukopenic f.** A hypothetical substance postulated to occur in inflammatory conditions as a result of cell death, and causing reduction in number of blood leukocytes. Endotoxin, derived from bacterial cell walls, is a well-defined leukopenic factor. **liver f.** A factor in liver that was found to cause remissions of pernicious anemia. Its purified form is vitamin $B_{12}$. **liver filtrate f.** PANTOTHENIC ACID. **LLD f.** VITAMIN $B_{12}$. **lupus erythematosus f.** ANTINUCLEAR ANTIBODY. Lu-

**teinizing hormone releasing f.** GONADOTROPIN RELEASING HORMONE. Abbr. LHRF, LRF **lymph node permeability f.** A substance derived from extracts of lymph nodes having the capacity to increase the permeability of vessels. Abbr. LNPF **lymphocyte-activating f.** INTERLEUKIN-1. **lymphocytosis-promoting f.** A protein product of *Bordetella pertussis* that stimulates lymphocyte production and may be responsible for other toxic effects. **macrophage-activating f.** A lymphokine that enhances phagocytic, bactericidal, and tumoricidal activities of macrophages. **macrophage chemotactic f.** A lymphokine that stimulates migration of macrophages. **macrophage migration inhibition f.** MIGRATION INHIBITION FACTOR. **maturation f.** Any substance, real or hypothetical, which can cause differentiation or maturation of a cell. **melanocyte inhibiting f.** MELATONIN. **melanocyte stimulating hormone release inhibiting f.** MELANOCYTE STIMULATING HORMONE INHIBITORY HORMONE. **migration inhibition f.** A protein of approximately 70 000 daltons released from sensitized lymphocytes and which inhibits the mobility of macrophages. Also *macrophage migration inhibition factor.* Abbr. MIF **milk f.** MOUSE MAMMARY TUMOR VIRUS. **mitogenic f.** A substance that stimulates transformation, DNA synthesis, and mitosis in immunocompetent lymphocytes. **modifying f.** MODIFYING GENE. **mouse antialopecia f.** INOSITOL. **mouse mammary tumor f.** MOUSE MAMMARY TUMOR VIRUS. **müllerian regression f.** A protein hormone secreted by the Sertoli cells of the fetal testis. The hormone induces the normal involution of the embryonic müllerian duct structures in the male. Also *müllerian duct inhibiting factor.* **multiple f.'s** Two or more genetic loci, the individual actions of which cannot be separated from their cooperative action in producing a recognizable character. **nerve growth f.** A specific protein which causes cells of embryonic spinal ganglia to send out axons. Snake venom and submaxillary salivary glands of mice contain very potent nerve growth factors. **neutrophil chemotactic f.** A lymphokine that stimulates migration of neutrophils. **osteoclast activating f.** A lymphokine that stimulates osteoclasts thus causing resorption of bone. **Passovoy f.** A coagulation activation factor that acts near factor XI in the coagulation cascade. **plasma thromboplastin f.** Any intrinsic coagulation plasma factor that promotes acceleration of the conversion of prothrombin to thrombin. Three such factors are recognized: factors VIII, IX, and XI. **platelet f.** Any of several substances that are primarily located within platelets or on their surface membranes and that contribute to coagulation by affecting platelet aggregation, adhesion, or retraction, or accelerate conversion of prothrombin to thrombin. Adsorbed substances are not considered platelet factors. Seven platelet factors are recognized. • Whereas coagulation factors are assigned Roman numerals, platelet factors are assigned Arabic numerals 1–7. **platelet activating f.** Acetyl glyceryl ether phosphorylcholine, a substance released by neutrophils, monocytes, mast cells, and basophils that causes platelets to aggregate and release $\beta$-thromboglobulin, 5-hydroxytryptamine, and platelet factor 4. **platelet derived growth f.** A heat-stable protein having a molecular weight of 13 000, which is contained in the $\alpha$-granules of platelets. It stimulates proliferation of smooth-muscle cells in tissue culture. Abbr. PDGF **Prower f.** FACTOR X. **quality f.** A number which relates the relative biologic effect of different types of radiation and is used in the field of radiation protection. The International Commission on Radiological Protection has assigned the quality factor values of from 1 to 20, depending on the linear energy transfer, defined in terms of the collision stopping power. Multiplying the absorbed dose in rads by the quality factor gives the dose in rems. Symbol: Q **R f.** Any of a large group of plasmids characterized by the presence of genes that cause resistance to various antimicrobial agents, mostly by coding for enzymes that inactivate the agent. Factors are classified in terms of incompatibility group or in terms of their pattern of resistance genes. Also *resistance factor, R plasmid.* See also FERTILITY INHIBITION. **rat acrodynia f.** PYRIDOXINE. **reducing f.** VITAMIN C. **resistance f.** R FACTOR. **resistance transfer f.** The part of a resistance plasmid, sometimes found alone, that codes for its own replication and machinery of conjugation. Combined with R-determinants, which code for enzymes that inactivate various antimicrobial agents, it becomes a resistance factor (R factor). Abbr. RTF **Reynals f.** HYALURONIDASE. **Rh f.** RH ANTIGEN. **Rhesus f.** RH ANTIGEN. **rheumatoid f.** An immunoglobulin, usually pentameric IgM but sometimes monomeric IgM or IgG, that is defined by its reactivity with the Fc portion of IgG. Rheumatoid factor is commonly present in the serum of patients with rheumatoid arthritis. **f. rho** The transcription termination factor, which promotes release of RNA polymerase from DNA. Its deficiency in mutants results in suppression of operon polarity. **risk f.** In epidemiology, an attribute or circumstance associated with an enhanced risk of developing or of dying from a specific disease. **ristocetin f.** FACTOR VIIIR:AG. **f. S** BIOTIN. **secretor f.** 1 A genetically-determined agent responsible for the secretion in body fluids of water-soluble A, B, or H substances, corresponding to the ABO type of the individual. Individuals who inherit the factor are secretors, those lacking it are nonsecretors. 2 SECRETOR. **sex f.** CONJUGATIVE PLASMID. **sigma f.** One of the subunits of bacterial DNA-directed RNA polymerase. It binds to the rest of the enzyme and enables it to bind to a promoter site in DNA while diminishing its affinity for the rest of the DNA. The sigma factor functions only during the initiation of a new RNA chain, after which it is released and recycled to another RNA polymerase. **skin f.** BIOTIN. **skin reactive f.** A lymphokine that causes local cutaneous inflammatory reactions. **somatotropin-releasing f.** GROWTH HORMONE RELEASING HORMONE. **specific macrophage arming f.** A lymphokine that causes macrophages to be cytotoxic for tumor cells. **spreading f.** HYALURONIDASE. **stable f.** FACTOR VII. **Stuart f.** FACTOR X. **Stuart-Prower f.** FACTOR X. **sulfation f.** *Outmoded* SOMATOMEDIN. **T-cell growth f.** INTERLEUKIN-2. **T-cell replacing f.** A lymphokine that augments antiheterologous erythrocyte plaque-forming cell responses. **termination f.** TERMINATION SEQUENCE. **thyroid stimulating hormone releasing f.** THYROTROPIN RELEASING HORMONE. Abbr. TSH-RF **thyrotoxic complement-fixation f.** One of several abnormal proteins found in the serum of patients with Graves disease. Its presence provides support for an autoimmune basis of this type of hyperthyroidism. **tissue plasminogen f.** TISSUE PLASMINOGEN ACTIVATOR. **transfer f.** 1 An activity found in the dialysate of leukocyte extracts from subjects who show delayed hypersensitivity to an antigen which is claimed to confer, when injected into other human subjects who are believed not to have encountered the antigen concerned, the specific delayed hypersensitivity to that antigen. 2 Single breath carbon monoxide diffusing capacity per unit lung volume. A British term. • Transfer factor is calculated and expressed in the Ameri-

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